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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/018,349 | 12/19/2001 | Yasuki Kato | 5.1195 | 1803 |

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FITZPATRICK CELLA HARPER & SCINTO
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112

| EXAMINER | |
|---|---|
| KISHORE, GOLLAMUDI S | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1615 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/018,349 | KATO ET AL. | |
| | Examiner | Art Unit | |
| | Gollamudi S. Kishore, Ph.D | 1615 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *16,19,20,35,42-44,49 and 50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16, 19-20, 35, 42-44 and 49-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

The amendment dated 6-12-07 is acknowledged.

Claims included in the prosecution are 16, 19-20, 35, 42-44 and 49-50.

*Claim Rejections - 35 USC § 103*

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 16, 19-20, 35, 42-44 and 49-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 850,646 of record by itself or Woodle 633 cited in the previous action.

EP discloses liposome formulations containing indolocarbazole (anti-cancer agent) derivatives. The liposomes are made from hydrogenated phospholipids and PEG-DSPE (note abstract, page 4, Examples and claims). Although, EP does not explicitly state that the sizes of the liposomes, on page 4, the reference teaches various methods of preparation of liposomes, either multilamellar or unilamellar and therefore, in the absence of showing the criticality, it is deemed obvious to one of ordinary skill in the art to prepare liposomes which are either multilamellar or unilamellar and of desired sizes

with the expectation of obtaining the best possible results. One of ordinary skill in the art would be motivated to prepare liposomes of instant sizes since the references of Woodle show the routine practice in the art of preparing liposomes of different sizes.

Applicant's arguments and the declaration have been fully considered, but are not found to be persuasive. Applicant argues that as shown in the Table 1 of the present specification, the liposomes of the present invention far more strongly inhibit the leakage of the indolocarbazole derivative from liposomes in biological components when compared to liposomes having an average particle size of 109 nm (.see Comparative Example 1), or when compared to liposomes comprising egg phosphatidylcholine or dipalmitoyl phosphatidylcholine (.see Comparative Examples 2 and 3, respectively). Applicant also argues that they showed that liposomes having an average particle size of 98 nm and liposomes comprising cholesterol easily leak the indolocarbazole derivative from the liposome in biological components (.see Comparative Examples 6 and 4, respectively, in the Declaration filed September 23, 2005). These arguments are not persuasive. First of all, for applicant to state that the instant claimed sizes are superior, they should compare instant compositions with prior art compositions and show that the prior art liposomes do not have claimed sizes. Applicant has not done that. Secondly, as previously pointed out the scope of the claims is not commensurate with the data shown in the declaration in terms of the sizes of upper limit of 500. With regard to even the lower limit of 120 nm (or even the upper limit of 500), a careful review of the results in Fig. 1 shows that there is no comparison was made between liposomes containing mixture of lipids and PEG-DSPE; instant claim 16

recites this combination. Furthermore, as previously pointed out, EP studies the encapsulation efficiencies of the liposomes over a period of time ranging from 0 to 24 hours and at various temperatures and determines that there is no leakage at all (see Table 3 on page 7).

3. Claims 16, 19-20, 35 and 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Woodle 633 or 556 or Allen (4,920,016) cited in the previous action in combination with EP cited above.

As discussed in the previous action, Woodle discloses a method of preparation of multilamellar vesicles (MLVs) containing a drug. The liposome sizes are 160 nm. The drugs include both steroidal and non-steroidal anti-inflammatory agents and anticancer agents. The liposomes are made from either hydrogenated soy phosphatidylcholine or PEG-DSPE (note the abstract, Examples, Example 4 in particular and claims).

Similarly, Woodle (556) discloses liposomes containing a drug. The liposome sizes are either 160 or 170 nm. The liposomes are made from either hydrogenated soy phosphatidylcholine or PEG-DSPE (abstract, Examples 4 and 7).

Allen (4,920,016) discloses liposomes made from DSPC and having a diameter of 170 nm. The active agents include anti-tumor agents and antibiotics (abstract, columns 10-11, Table 1 in Example 3).

What is lacking in Woodle 633, 556 or Allen 016 is the teaching of indolocarbazole derivatives as the active agent. However, it would have been obvious to one of ordinary skill in the art that any desired drug could be encapsulated within the liposomes based on the guidance provided by Woodle, especially in view of EP which

teaches the knowledge in the art of encapsulation of this compound in the liposomes. One of ordinary skill in the art would expect similar encapsulation.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that Woodle, and Allen only teach the retention of their liposomes in blood, but do(es) not each or suggest inhibition of leakage of any liposomes in the presence of biological product. This argument is rather confusing since instant composition and the prior art composition are administered to subjects and therefore, one would consider that blood taught by the prior art is closer to a biological system than plasma used in instant examples. Furthermore, instant claims are composition claims and are not drawn to a method of preventing leakage of the liposomes in a biological product.

4. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Woodward Michael can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ Gollamudi S Kishore /

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK